

## SPECIAL ARTICLES

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### PHYSIOLOGIC ASPECTS OF SCHIZOPHRENIC WITHDRAWAL

A. ANGYAL, M.D.

H. FREEMAN, M.D.

AND

R. G. HOSKINS, M.D.

WORCESTER, MASS.

So far as theoretic orientation is concerned, exclusively "psychogenic" or exclusively "organogenic" attitudes in psychiatry are definitely on the decrease. While American psychiatry, in particular, is broad minded enough to acknowledge the significance of interacting organic, psychologic and social factors in the genesis and the perpetuation of mental disorders, nevertheless much remains to be done in the synthesis of facts of apparently different orders that are obtained by the use of the technics of the physiologist, the psychologist and the sociologist, respectively. So great are the methodologic difficulties that it is to be feared that many workers, consciously or otherwise, don mental blinders as a defense against the complexities of the problems. Thus, while admitting the desirability and even the necessity of a synthetic approach, they too often carry on their individual studies in a single domain to the practical exclusion of attention to other domains.

To a considerable extent the unilateral approaches can be justified as means of bringing to bear special varieties of technical competence. Nevertheless, the meaning of such partial findings is likely to be mostly lost except as the data are successfully embodied in the larger whole. The inner unity—the connectedness—of the phenomena must somehow be found and reflected in the appraisal of the net meaning of the data. The outstanding task of psychiatry today is to evolve a methodology for such syntheses. A step toward this end is to recognize parallel or common meanings in the data derived from different approaches. In this paper we wish to point out what seems to us a rather meaningful connection between certain features in the psychology and the physiology of schizophrenia.

It is generally recognized that in spite of the great variety of clinical pictures in the schizophrenic group of disorders, one symptom is common to all of them. This is the schizophrenic withdrawal. Psychologically,

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From the Research Service of the Worcester State Hospital.

withdrawal means that the vital relations between a person and his physical and social environment become less intense and less numerous. Since life processes consist of interactions between the person and his environment, the consequence of a partial break in environmental contacts leads to an impoverishment and diminished intensity of living. This aspect of schizophrenic withdrawal is expressed psychologically in lack of interest, apathy and indifference. However, the life of the schizophrenic person runs at a low ebb not only psychologically but also physiologically. This is manifested in a lowering of the basal levels of various physiologic functions, such as the basal oxygen consumption rate, basal blood pressure and circulation time.

The lessening of interaction between the person and his environment in schizophrenia becomes particularly evident when he is exposed to the influence of various stimuli. The reduction of responses to stimuli emanating from the physical and social environment is well known in the psychology of schizophrenia. We wish to present evidence that a diminution of responsiveness is paralleled also in the physiology of schizophrenia. This may be illustrated by certain findings obtained in our laboratories.

Our data thus far obtained on the physiologic hyporeactivity of the schizophrenic patient pertain to three major fields: general metabolism, functions of the autonomic nervous system and functions of the central nervous system.

*Hyporeactivity to Metabolic Stimulants.*—The response of the schizophrenic organism to metabolic stimulation is less than normal, so that to induce a comparable reaction excessive doses are necessary. In a therapeutic experiment, Hoskins and Sleeper<sup>1</sup> administered as much as 48 grains (3 Gm.) daily of desiccated thyroid substance to a patient with little apparent physiologic reaction. Following this lead, Cohen and Fierman<sup>2</sup> administered thyroid to 8 schizophrenic patients in doses of 15 to 18 grains (1 to 1.2 Gm.) daily for several months. Despite an increase in the oxygen consumption rate from a premedication level of 95 to 141 per cent of prediction, the pulse rate tended to decrease once a maximal level of 110 had been reached. No ill effects from the large doses of thyroid were observed. No excessive perspiration, tremor or gastrointestinal disturbance was noted. The psychiatric-clinical changes observed during the period of hyperthyroidism were slight.<sup>3</sup>

1. Hoskins, R. G., and Sleeper, F. H.: A Case of Hebephrenic Dementia Praecox with Marked Improvement Under Thyroid Treatment, *Endocrinology* **13**:459, 1929.

2. Cohen, L. H., and Fierman, J. H.: Metabolic, Cardiovascular, and Biochemical Changes Associated with Experimentally Induced Hyperthyroidism in Schizophrenia, *Endocrinology* **22**:548, 1938.

3. Cohen, L. H.: Psychiatric Changes Associated with Induced Hyperthyroidism in Schizophrenia, *Psychosom. Med.* **1**:414, 1939.

The reduced metabolic reactivity is not restricted to a specific endocrine substance but is present also on administration of dinitrophenol, which is a general oxidative stimulant. After the administration of 300 mg. of dinitrophenol to 20 schizophrenic patients and a comparable number of normal controls, Freeman <sup>4</sup> found that the response in cutaneous temperature, insensible perspiration rate and oxygen consumption rate was less in the patients.

*Hyporeactivity of the Autonomic Nervous System.*—A lessened degree of reactivity was also noted in the field of autonomic physiology. The increase in blood pressure and pulse rate induced by the intravenous administration of 0.05 mg. of epinephrine hydrochloride was definitely less in schizophrenic patients than in normal subjects.<sup>5</sup>

Marked differences in autonomic responsiveness between schizophrenic and normal persons were found by Freeman and Rodnick.<sup>6</sup> These investigators induced experimentally a rather severe stress situation by having the subjects breathe hot moist oxygen, thus blocking the loss of heat from the lungs. They found that the response in blood pressure, heart rate and respiratory volume was markedly less in schizophrenic patients than in normal subjects. The reaction to this stress situation was in more than one fourth of the normal controls so alarming that the experiment could not be completed, while the patients gave little sign of any discomfort.

*Hyporeactivity of the Central Nervous System.*—A depression of reactivity referable to the central nervous system was found by Angyal and Blackman,<sup>7</sup> who studied the nystagmic response to vestibular stimulation in 20 normal and 58 schizophrenic subjects. Both caloric and rotatory stimulations were applied. The variables which they studied were the absolute number and the frequency of nystagmic beats,  $\frac{\text{(number of nystagmic beats)}}{\text{(total duration of reaction)}}$ . In response to rotatory stimulation they found a 21 per cent reduction in the absolute number and a 26.2 per cent reduction in the frequency of nystagmic beats. In response to caloric stimulation the schizophrenic patients showed a 38.8 per cent reduction

4. Freeman, H.: Heat-Regulatory Mechanisms in Normal and Schizophrenic Subjects Under Basal Conditions and After the Administration of Dinitrophenol, *Arch. Neurol. & Psychiat.* **43**:456 (March) 1940.

5. Freeman, H., and Carmichael, H. T.: A Pharmacodynamic Investigation of the Autonomic Nervous System in Schizophrenia: I. Effect of Intravenous Injections of Epinephrine on the Blood Pressure and Pulse Rate, *Arch. Neurol. & Psychiat.* **33**:342 (Feb.) 1935.

6. Freeman, H., and Rodnick, E. H.: Autonomic and Respiratory Responses of Schizophrenic and Normal Subjects to Changes of Intra-Pulmonary Atmosphere, *Psychosom. Med.* **2**:101 (April) 1940.

7. Angyal, A., and Blackman, N.: Vestibular Reactivity in Schizophrenia, *Arch. Neurol. & Psychiat.*, this issue, p. 611.

in the frequency and a 48.3 per cent reduction in the absolute number of nystagmic beats.

The results of a recent study by Rodnick<sup>8</sup> also indicated a diminished responsivity of the central nervous system. He studied the difference of response in cutaneous resistance in schizophrenic and in normal subjects. The response to a strong auditory stimulus did not differ to any great extent in the two groups. The preparatory response of the patients to the "ready" signal, however, was only half that of the normal subjects.

Besides our own data, results obtained by other workers also seem to support our thesis of general reduction of responsiveness in schizophrenic patients. We shall refer only to two such findings. Fischer<sup>9</sup> reported that in 277 cases of schizophrenia the specific dynamic action of protein (increase in basal metabolic rate after ingestion of meat) was diminished.

Meco<sup>10</sup> observed that during treatment with various thermogenic agents, mainly foreign proteins and other chemical substances, the rise in temperature in the schizophrenic group was far below that in other groups, and that the whole "thermic shock" was much diminished in the schizophrenic patients.

#### SUMMARY

Summarizing, we may say that in schizophrenia a rather general reduction of physiologic responsiveness is present. The reaction to metabolic stimulants, such as thyroid and dinitrophenol, was definitely diminished. The reaction to epinephrine administered intravenously as well as to the blocking of heat loss through the lungs was definitely less in schizophrenic patients than in normal persons, indicating reduction of autonomic responsiveness. The nystagmic response to rotation and to caloric stimulation was greatly diminished. The change in cutaneous resistance in response to a preparatory stimulus was far below the normal.

We are not prepared to state whether psychologic withdrawal is caused by a physiologic withdrawal (hyporeactivity) or vice versa. It is probable that neither is the case, but that one is dealing with withdrawal of the total personality manifested in a variety of psychologic and physiologic characteristics.

8. Rodnick, E. H.: A Comparison of Schizophrenic and Normal Subjects with Respect to Two Measures of Autonomic Reactivity: Weight Loss and Galvanic Skin Response, to be published.

9. Fischer, S.: Gasstoffwechselveränderungen bei Schizophrenen; Bericht über 345 Kranke (277 Schizophrenie, 68 Depressive), *Ztschr. f. d. ges. Neurol. u. Psychiat.* **147**:109, 1933.

10. Meco, O.: L'esistenza e l'interpretazione di una scarsità di reazione piretica nei dementi precoci, *Riv. di pat. nerv.* **44**:677, 1934.

The question may justly be asked: What value may be derived by bringing together a number of physiologic facts under the common heading of decreased responsiveness and, further, by tying up all these features with psychologic withdrawal? The possible value of such an attempt may be summarized in the following points.

1. It may well be that, for instance, a diminished response to thyroid and a diminished response to vestibular stimulation are distinct phenomena, with no relation at all between them. Furthermore, it is possible that there is only a superficial analogy between those instances of reduced physiologic resistiveness which we have cited and the various psychologic symptoms grouped in the category of withdrawal. On the other hand, it may also be true that there is a significant and meaningful connection between all these features. In other words, it is possible that what is observed in schizophrenia is not resistance to thyroid medication, a lessened response to epinephrine, a diminished vestibular reactivity and psychologic indifference to stimuli of the physical and social environment, but only manifestations of one and the same condition. It may be useful to broaden the concept of withdrawal to designate not a purely psychologic but a "holistic" or "psychobiologic" phenomenon. The possibility that this phenomenon may be holistic and not segmental is strong enough to permit this assumption to be used as a working hypothesis.

2. The type of approach which we are suggesting here should not be a retreat into generalities. On the contrary, we wish to emphasize the necessity of specific and concrete studies. After a number of psychologic and physiologic features are brought together under the common concept of withdrawal, this concept, which is used at present with a somewhat vague and general connotation, gains a new and rather definite meaning. The phenomenon of withdrawal may thus be specifically defined as consisting of such and such psychologic and physiologic characteristics.

3. The assumption of a psychobiologic disturbance, characterized by certain psychologic and physiologic manifestations, raises new problems and gives specific hints for further studies. It makes a distinct difference with regard to the type of problems one investigates whether one works with this or with some other hypothesis. This may be illustrated by a hypothetical example. Once the resistance of the schizophrenic person to thyroid medication is established, one may attempt to study systematically whether this phenomenon is due to (1) disturbed absorption, (2) some chemical agent in the blood which may neutralize thyroxine or (3) tissue resistance. That is, one may study resistance to thyroid as such. This type of investigation is necessary, and it should be made in every instance. However, if one is oriented along

the lines featured, further investigations are also indicated. One not only should study decreased reaction to thyroid as such but also should consider the possibility that this phenomenon is a manifestation of a generalized condition of reduced reactivity. The latter being assumed, the first task will be to determine what functions are involved and to what degree. Our studies already indicate that the reduction of reactivity in persons with schizophrenia is not uniform; one physiologic function undergoes a greater reduction than another; some functions remain unchanged, and in some respects the reactivity may even be increased. The last possibility was suggested, for example, by Freeman and Hoskins'<sup>11</sup> finding of an increased response of the blood pressure to a preparation of adrenal cortex. The increase of blood lipids after testosterone medication observed by Randall<sup>12</sup> might be of the same order. Therefore, the reduction of responsiveness, since it does not involve all functions of the organism uniformly, will probably be most adequately presented in the form of a profile, which would indicate what functions are involved and to what degree. After such a profile has been obtained and the essential psychologic and physiologic components of withdrawal have been defined, one will be better equipped to investigate the causation of this complex phenomenon.

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11. Freeman, H., and Hoskins, R. G.: Comparative Sensitiveness of Schizophrenic and Normal Subjects to Glycerin Extract of Adrenal Cortex, *Endocrinology* **18**:576, 1934.

12. Randall, L. O.: Effect of Testosterone on Serum Lipids in Schizophrenia, *J. Biol. Chem.* **133**:137, 1940.